

REMARKS*Claim Rejections - 35 USC § 112 First Paragraph*Rejection withdrawn

The Applicant notes that the rejection of claims 22, 23, and 25-28 under 35 USC § 112, second paragraph as indefinite because of recitation of the phrase “penetration enhancer” and “shear-thinning polysaccharide gum” in Claim 22 has not been reiterated, and is hence deemed withdrawn.

New Rejection

Claims 22, 23, 25, 27 and 28 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner could not find support for the language “wherein application of the semi-solid composition produces an increase in blood flow through the region of vasospasm within thirty minutes of the application” in the specification.

The Applicant respectfully traverses this rejection. Support can be found in the application as filed at least as follows:

- Return of vessel diameter to pre-vasospasm diameter:
 - Page 35, Table 3
 - Fig. 3
 - Page 37, lines 1-9, including Table 4
- Return of vascular perfusion volume (ml/min) to pre-vasospasm value:
 - Page 6, lines 24-25. This corresponds to paragraph [0019] of the published application US20050009918A1.
 - Page 40, including Table 6, where local blood flow was measured by laser Doppler flowmetry.
 - Fig. 4
 - Page 44, including Table 9
- Use during surgery to treat local vasospasm (after application to the vascular extima, a currently non-elected species):
 - Example 4, where local blood flow as measured as blood flow velocity and vessel diameter using ultrasonography
 - Page 44, including Table 9.
 - Fig. 6
 - Example 5, especially page 47,
 - Page 45, lines 16-22, including Table 11
 - Page 48, line 21 to page 49, line 3

The Applicant respectfully submits that adequate support is found in the specification as filed. The rejection of claims 22, 23, 25, 27 and 28 under 35 U.S.C. §112, first paragraph is unwarranted and should be withdrawn.

Claim Rejection - 35 USC § 102

Claims 22, 23, 25, and 28 have been rejected under 35 USC §102(b) as anticipated by Buyuktimkin et al. (US 6,046,244). The rejection is traversed. The Office Action states "The recitation in the amended claim of "where application of the semisolid composition produces an increase in blood flow through the region of vasospasm within thirty minutes of the application" is effect of the composition and the application of the composition of Buyuktimkin would inherently produce the effect within the time recited. Buyuktimkin meets the limitations of the claims." (Emphasis added).

In order to effectively anticipate a claim, a reference must teach each and every limitation of the claim. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). First, the Buyuktimkin reference does not contain the word "vasospasm." Second, the Buyuktimkin reference is silent on the issue of whether the disclosed compositions would have an effect on blood vessel diameter within 30 minutes of being applied to tissue. The working examples in the Buyuktimkin reference disclose *in vitro* studies on a model system, specifically, shed snake skin in Franz-type diffusion cells (column 8, line 60 to column 9, line 23), in which the amount of prostaglandin E₁ that crosses the snake skin 1-4 hours after application is measured. There is no disclosure of the amount of prostaglandin E₁ that might be transported across the snake skin at time points earlier than one hour. There is no disclosure or suggestion of how the results from this *in vitro* system might relate to the application of such compositions *in vitro* to a living subject, and whether an effective amount of prostaglandin E₁ might be transported across living skin into the underlying vascularized tissue and affect blood flow through the vascularized tissue within 30 minutes.

The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).

“[T]he examiner must provide some evidence or scientific reasoning to establish the reasonableness of the examiner's belief that the functional limitation is an inherent characteristic of the prior art” before the burden is shifted to the applicant to disprove the inherency. *Ex parte Skinner*, 2 USPQ2d 1788, 1789 (Bd. Pat. App. & Int. 1986). *See also, Ex parte Whalen*, 89 USPQ2d 1078, 1083 (Bd. Pat. App. & Int. 2008) (rejection reversed where the Examiner did not provide evidence or scientific reasoning).

In the present case, the Examiner has not presented any evidence or scientific reasoning, only a conclusory statement that the Buyuktimkin reference meets the limitations of the claims. The rejection of claims 22, 23, 25, and 28 under 35 USC § 102(b) as anticipated by Buyuktimkin et al. (US 6,046,244) is unwarranted and should be withdrawn.

Claim Rejection - 35 USC §103(a)

Claims 22, 23, 25, 27 and 28 have been rejected under 35 USC §103(a) as unpatentable over Buyuktimkin et al. (US 6,046,244) in view of Clifford et al. (Br. Med. J. 1980 October 18; 281(6247): 1031-1034). The Applicant respectfully traverses the rejection.

As discussed above, the Buyuktimkin reference neither explicitly nor inherently discloses “wherein application of the semi-solid composition produces an increase in blood flow through the region of vasospasm within thirty minutes of the application.” The Applicant respectfully submits that the combination of the Buyuktimkin reference and the Clifford reference neither discloses or suggests the claimed invention as a whole.

The Clifford reference describes an *in vivo* study of human patients having severe vasospastic disease of the hands. The patients were admitted to hospital and prostaglandin E₁ was administered intravenously through a central venous cannula over 72 hours (page 1031, right column). The patients received prostaglandin E₁ intravenously in physiological saline at a dose of 6 ng/kg/min which was increased after 12 hours in the absence of side effects to 10 ng/kg/min (page 1032, left column). Measurements were made immediately before, during, and 24 hours after the infusion and again two and six weeks later. *Ibid*. The Clifford reference does not state when the “during” measurements were made during the 72 hour intravenous administration of prostaglandin E₁ to the entire subject. Thus, while the combination of the Buyuktimkin reference and the Clifford reference disclose the treatment of a subject in need of treatment for vasospasm, the administration of the prostaglandin E₁ occurs over the period of hours to days. Thus, the combination of the Buyuktimkin reference and the Clifford reference neither disclose or suggest the present invention of the treatment of vasospasm using the topical application to a region of the subject's tissue of an effective amount of a semi-solid composition comprising a vasoactive prostaglandin, wherein the application of the semi-solid composition produces an increase in blood flow

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through the region of vasospasm within thirty minutes of the application. The Applicant respectfully submits that the rejection of claims 22, 23, 25, 27 and 28 under 35 USC §103(a) as unpatentable over Buyuktimkin et al. (US 6,046,244) in view of Clifford et al. (Br. Med. J. 1980 October 18; 281(6247): 1031-1034) is unwarranted, and should be withdrawn.

Conclusion

In light of the arguments presented herein, the Applicant respectfully submits that all pending claims are in condition for allowance and requests a timely Notice of Allowance to follow in this case. The Applicant requests that the Examiner telephone the undersigned at (508) 860-1472 in the event that a telephone discussion would be helpful in advancing the prosecution of the present case.

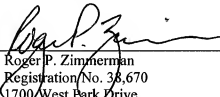
A Request for Continued Examination and a petition for a three-month extension of time and the required fees are submitted herewith. It is believed that no additional fees or extensions of time are required. In the event any additional extensions of time are necessary, please consider this a petition therefor. In the event any fees or credits are due, the undersigned hereby authorizes the fees or credits to be charged to Deposit Account No. 50-1582.

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Respectfully submitted,

MIRICK O'CONNELL DEMALLIE & LOUGEE, LLP

By



Roger P. Zimmerman
Registration No. 38,670
1700 West Park Drive
Westborough, MA 01581
Telephone – 508-898-1501
Facsimile – 508-898-1502